

July 17, 2002

Elizabeth Hunt  
Executive Director  
Mercaptans/Thiols Council  
941 Rhonda Place S.E.  
Leesburg, VA 20175

Dear Ms. Hunt:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the methyl mercaptans analogs category, posted on the ChemRTK Web Site on December 18, 2001. I commend the Mercaptans/Thiols Council (MTC) for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Chemical RTK HPV Challenge Program website EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the attached Comments on the Chemical RTK web site within the next few days. As noted in the comments, we ask that MTC advise the Agency, within 60 days of the posting on the Chemical RTK website, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit general questions about the HPV Challenge Program through the Chemical RTK web site comment button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at [tsca-hotline@epa.gov](mailto:tsca-hotline@epa.gov).

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

Oscar Hernandez, Director  
Risk Assessment Division

Attachment

cc: W. Sanders  
A. Abramson  
C. Auer  
M. E. Weber

**EPA Comments on Chemical RTK HPV Challenge Submission:  
Methyl Mercaptans Analogs Category**

**Summary of EPA Comments**

The Sponsor, the Mercaptans/Thiols Council, submitted a test plan and robust summaries to EPA for the methyl mercaptans analogs category composed of methyl mercaptan [methanethiol, CH<sub>3</sub>SH (CAS No. 74-93-1)] and methanethiol, sodium salt [methyl mercaptide, CH<sub>3</sub>SNa (CAS No. 5188-07-8)] dated December 5, 2001. EPA posted the submission on the ChemRTK HPV Challenge Web site on December 18, 2001.

EPA has reviewed this submission and has reached the following conclusions:

1. Category Justification. The submitter provided an adequate justification that methyl mercaptan and methyl mercaptide are interchangeable with regard to their toxicity because methyl mercaptide is expected to be rapidly converted to methyl mercaptan in biological and environmental systems.
2. Physicochemical Properties and Environmental Fate Data. The submitter needs to provide a discussion or robust summaries for the vapor pressure and water solubility endpoints and revise the melting and boiling point values for methyl mercaptide in the test plan.
3. Health Endpoints. For the reproductive and developmental toxicity endpoints, the submitter provided data for hydrogen sulfide as an analog for methyl mercaptan and methyl mercaptide. EPA considers this analogy not acceptable for the following reasons: 1) there is no quantitative evidence that methyl mercaptan is converted to hydrogen sulfide; 2) developmental toxicity results for the submitted study differ from other available data; and 3) hydrogen sulfide is a known neurotoxicant and its mechanism of toxicity may differ from methyl mercaptide. EPA considers that the reproductive and developmental toxicity endpoints have not been adequately addressed.
4. Ecotoxicity. EPA agrees with the sponsor's proposal that an acute fish toxicity study and an algal inhibition study for methyl mercaptide are necessary to address these endpoints.

EPA requests that the Submitter advise the Agency within 60 days of any modifications to its submission.

**EPA Comments on Methyl Mercaptans Analogs Challenge Submission**

**Category Definition**

The submitter proposed methyl mercaptan (also known as methanethiol) and its sodium salt, methyl mercaptide (also known as sodium methanethiolate, sodium thiomethoxide, or methanethiol, sodium salt), as a category. The submitter considered a non-sponsored chemical, hydrogen sulfide, as an analog for these chemicals and provided its reproductive/developmental toxicity data to address these endpoints. The category description is clear and unambiguous.

**Category Justification**

The submitter proposed methyl mercaptan and methyl mercaptide as a category based on a common functional group and a "family approach" for justifying the grouping of acids and their corresponding salts under a category. With a pKa of 10.7 for the methyl mercaptide anion, conversion of the conjugate base to

the free acid is on the order of 1,000-fold (ratio of 1:1000,  $\text{NaSCH}_3\text{:CH}_3\text{SH}$ ) at pH 7. Therefore, at the physiological pH and pHs commonly encountered in the environment, methyl mercaptide will be converted to methyl mercaptan. EPA agrees with the submitter's conclusion that toxicological information (ecotoxicity and health effects) for methyl mercaptide is equivalent to that of methyl mercaptan.

### **Test Plan**

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

*Methyl mercaptan:* Adequate data are available for all endpoints for the purposes of the HPV Challenge Program. However, the submitter needs to revise values for melting point and boiling point (see Specific Comments on the Robust Summaries).

*Methyl mercaptide:* Adequate data are available for the purposes of the HPV Challenge Program. The test plan (page 7) discusses the results for vapor pressure and water solubility; however, robust summaries are not provided for these endpoints.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

Adequate data are available for all endpoints for the purposes of HPV Challenge Program.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Adequate data are available for acute toxicity, repeated-dose toxicity, and genetic toxicity on methyl mercaptan and methyl mercaptide for the purposes of HPV Challenge Program.

*Reproductive/Developmental Toxicity.* The submitter provided hydrogen sulfide data for these endpoints and proposed that these data be used as analog data representative of methyl mercaptan. The submitter states that acute toxicity and metabolism data generally indicate similarities between hydrogen sulfide and methyl mercaptan with respect to both toxicologic effects and metabolic disposition as support for the use of hydrogen sulfide as an analog. Given the data presented by the submitter, although conversion of methyl mercaptan to hydrogen sulfide via demethylation appears quantitatively possible, the majority of administered methyl mercaptan in rats is metabolized to a sulfate that is conjugated and eliminated via the urine. Thus, the evidence provided that methyl mercaptan converts to hydrogen sulfide is not strong. In addition, hydrogen sulfide is a known neurotoxicant and may have a different mechanism of toxicity than methyl mercaptan. Unless the submitter provides more information to strengthen this analogy, reproductive/developmental toxicity testing of methyl mercaptan needs to be conducted.

Finally, it should be noted that there are other data from the literature that show developmental effects (severe alterations in the Purkinje cell dendrite fields in rat pups) following exposure of pregnant rats to hydrogen sulfide during the gestational period (Hannah and Roth 1991).

### **Ecotoxicity**

*Fish and algae.* EPA agrees with the submitter's plan to conduct acute fish toxicity and algal inhibition studies with methyl mercaptide.

*Invertebrates.* Adequate data exist on invertebrate acute toxicity for the purposes of the HPV Challenge Program with the exception of some missing data elements.

## **Specific Comments on the Robust Summaries**

### **Physicochemical Properties**

*Methyl mercaptide: Melting point and Boiling point:* The test plan Table 4 indicates a melting point of 12 °C and a boiling point of >210 °C. However, on page 2 of 21 of the robust summaries the submitter provides a melting point value of >210 °C, and a boiling point value of 69 °C.

### **Health Effects**

*Repeat Dose Toxicity.* In the IUCLID data set for methyl mercaptan, the summary of the repeated-dose inhalation toxicity study would be improved by the addition of a concluding statement clearly indicating the adverse effect(s) associated with the NOAEL and LOAEL.

In the IUCLID data set for hydrogen sulfide, the summaries of the repeated-dose inhalation toxicity study appear to contain conflicting information regarding adverse effects and reported NOAELs and LOAELs. The adverse effect(s) associated with these levels should be clearly indicated.

### **Ecotoxicity**

*Daphnia.* The submitter needs to verify that the chemical tested in the key invertebrate study is a 32.9% solution of sodium methanethiolate.

## **Followup Activity**

EPA requests that the Submitter advise the Agency within 60 days of any modifications to its submission.

## **References**

Hannah RS, Roth SH. 1991. Chronic exposure to low concentrations of hydrogen sulfide produces abnormal growth in developing cerebellar Purkinje cells. *Neurosci Lett* 122:225-228.